

Embryonal Rhabdomyosarcoma and Chromosomal Breakage in a Newborn Infant With Possible Dubowitz Syndrome

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We report on a newborn girl with Dubowitz syndrome (DS) and embryonal rhabdomyosarcoma (ERMS), with multiple chromosomal breakage (MCB). The tumor was resected but recurred in a few months, resulting in the infant's death. Malignancy and chromosomal breakage have been reported previously in DS. However, ERMS has not been reported among the malignant tumors diagnosed in DS. To our knowledge, concurrence of DS, ERMS, and MCB has not been reported previously. This is the first observation of DS in the Arab ethnic group. Am. J. Med. Genet. 92:107–110, 2000.

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INTRODUCTION

Since its first description in 1965 [Dubowitz, 1965], more than 140 cases of Dubowitz syndrome (DS) have been reported [Tsukahara and Opitz, 1996]. The syndrome comprises intrauterine and postnatal growth retardation, eczema, microcephaly, mild to moderate mental retardation, hyperactivity, and short attention span. Facial appearance is characteristic. Overall, the condition may involve the cutaneous, ocular, dental,

digestive, musculoskeletal, urogenital, cardiovascular, neurological, hematological, and immune systems. A propensity to malignant disorders has been reported. Acute lymphoblastic leukemia, non-Hodgkin lymphoma, malignant lymphoma, and neuroblastoma, but not embryonal rhabdomyosarcoma (ERMS) were the malignant tumors reported in DS [Belohradsky et al., 1988; Grobe et al., 1983; Sauer and Spelger, 1977]. Spontaneous and postclastogenic stress chromosomal breakage is rare [Levin et al., 1987], but has been reported in three patients with DS [Thuret et al., 1991; Walter and Desposito, 1985]. Here, we describe DS, (multiple chromosomal breakage) MCB, and ERMS in a Saudi infant.

CLINICAL REPORT

The patient, a term newborn girl, was born to an 18-year-old Saudi mother whose antenatal fetal ultrasound studies at 24 weeks of gestation showed a 24-week growth retarded fetus with a soft tissue mass over the chest. The family history was unremarkable except for first-degree consanguinity between parents. The baby was delivered vaginally and at birth required minimal positive pressure ventilation. She had an Apgar score of 5 and 9 at one and five minutes, respectively.

Birth weight (2.11 kg), length (41 cm), and head circumference (29 cm) were all below the third centile, an indication of symmetrical intrauterine growth retardation. The infant had (Fig. 1) microcephaly with small anterior fontanel; hypoplastic supraorbital ridges; partial ptosis of right eye; left blepharophimosis; hypertelorism; apparently low-set deformed ears; high arched palate; micrognathia; broad nasal tip; sacral dimple; overriding toes; and bilateral pes planus. Seborrheic dermatitis was noted on the face and scalp (Fig. 1). She also had a large (10 × 15 cm) mass over the right hemithorax encroaching on the right shoulder (Fig. 2). The mass was rubbery, nontender, and not adherent to un-

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Fig. 1. Peculiar facial appearance with mild seborrhea.

derlying tissues. It was covered with skin with dilated and tortuous blood vessels. Chest computed tomography (CT) scan showed a lobulated soft tissue mass arising from the right chest wall muscle with a broad base. There was marked heterogeneous enhancement and areas of cystic necrosis in the mass (Fig. 3). The histopathology studies showed a malignant spindle cell sarcoma arranged in fascicles with foci of hemangiocy-toma-like vascular pattern (Fig. 4). The histological diagnosis was given as spindle cell sarcoma that was confirmed by electron microscopic findings of thick and



Fig. 2. The chest mass.

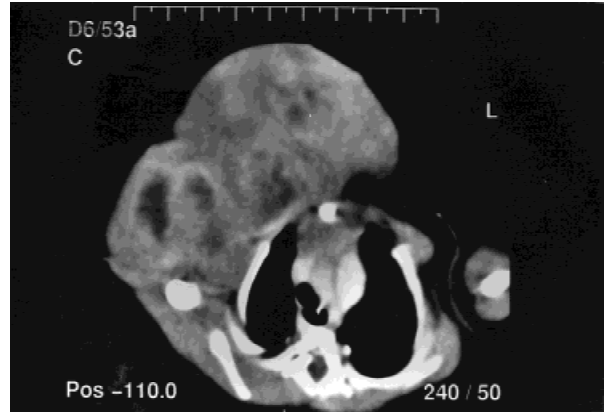


Fig. 3. CT scan of the chest showing the extrathoracic mass with cavi-tations.

thin filament and focal Z-band consistent with ERMS. The mass was resected. The infant had a transient leu-cocytosis (36.7×10^3 cells / μ L) and thrombocytopenia (35×10^3 cells / μ L) that resolved at the age of 12 days. The infant had normal (46, XX) chromosomes with multiple spontaneous breaks. Findings on echocardiogram, renal sonogram, electrocardiogram, TORCH screen, and skeletal survey were all unremarkable.

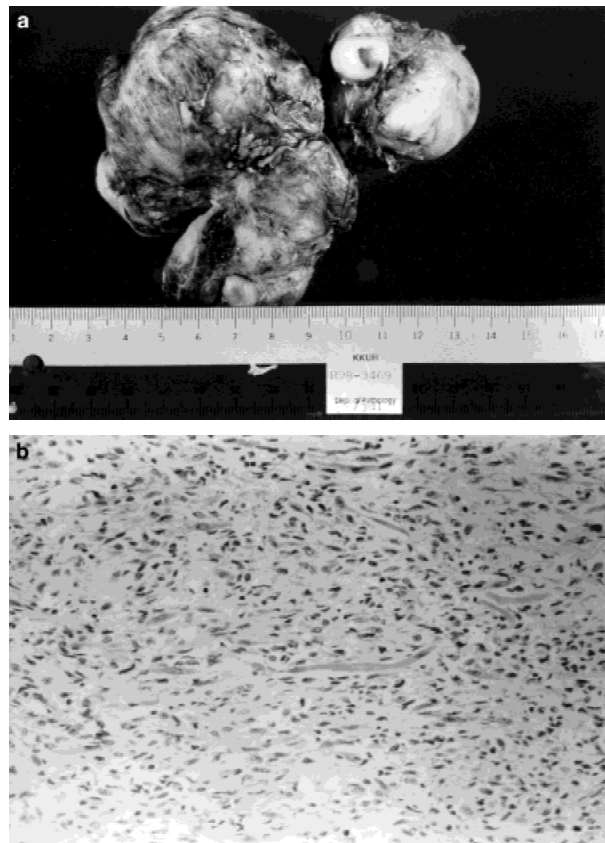


Fig. 4. **a:** Gross photograph showing a lobulated tumor with tan, fleshy and firm appearance. **b:** High-power microphotograph demonstrating few fusiform large cells with abundant eosinophilic cytoplasm (rhabdomyo-blasts), (hematoxylin-eosin, original magnification $\times 100$).

TABLE I. Reported Cases of Dubowitz Syndrome Associated With Malignancies

Malignancy	Sex	Age at diagnosis	Age at death	Reference
Malignant lymphoma	F	6 years	6 years	Sauer and Spelger [1977]
Neuroblastoma	F	3 years	3 years	Sauer and Spelger [1977]
Acute lymphoblastic leukemia	F	6 years	6 years	Grobe et al. [1983]
Non-Hodgkins lymphoma	M	16 years	?	Belohradsky et al. [1988]
Embryonal rhabdomyosarcoma	F	Birth	3 months	Present case

Both plain and three-dimensional CT brain scan showed lambdoid craniosynostosis, colpocephalic configuration of the lateral ventricles, and evidence of pachygyria (Fig. 5). Poor visual fixation at the age of 1 month with optic nerve atrophy and degenerative retinal changes were also observed. Otherwise, she had intact neonatal reflexes, but with poor sucking and swallowing. She was discharged home at 1 month of age on orogastric tube feeding. The infant died at the age of 3 months with recurrence of the ERMS.

DISCUSSION

DS is probably underreported in the Arab ethnic population, since this is the first case reported in such ethnic group known to have a very high consanguinity rate [El-Badramany et al., 1997; Salih, 1997].

Our patient had the classical findings of DS. However, some of the previously reported anomalies were

absent. Other defects such as lambdoid craniosynostosis, present in this patient, were not described previously. These were probably secondary to abnormal brain growth as evidenced by the colpocephalic configuration of the lateral ventricles on cranial CT scans, and presence of pachygyria, suggesting an associated brain migration disorder. Also, the association of spontaneous chromosomal breakage and congenital rhabdomyosarcoma has not been reported previously. However, the presence of spontaneous and induced chromosomal breakage in DS in association with hematological and immunological abnormalities is well-recognized [Thuret et al., 1991; Walter and Desposito, 1985]. Although chromosomal analyses have been performed frequently on cases with DS and have revealed a normal pattern in 77 cases analyzed, studies on chromosome instability have been performed infrequently, and the association of DS with chromosomal instability remains unresolved [Tsukahara and Opitz, 1996]. Spontaneous chromosome breakage was slightly increased in one of two sibs [Walter and Desposito, 1985], and a high breakage rate after clastogenic stress was observed in two sibs who had leukopenia and recurrent neutropenia and agranulocytosis [Thuret et al., 1991]. Our patient had transient thrombocytopenia with no other hematological or immunological disorder at the time of presentation.

The other striking finding in our patient is the presence of a congenital malignant tumor. No previously reported cases of DS with malignant disorders were congenital, but developed during childhood; and none of those tumors was an ERMS (Table I). The prognosis of the syndrome with associated malignancy is poor, since all cases died immediately or soon after diagnosis, including our patient, who died at the age of 3 months from recurrence of the tumor.

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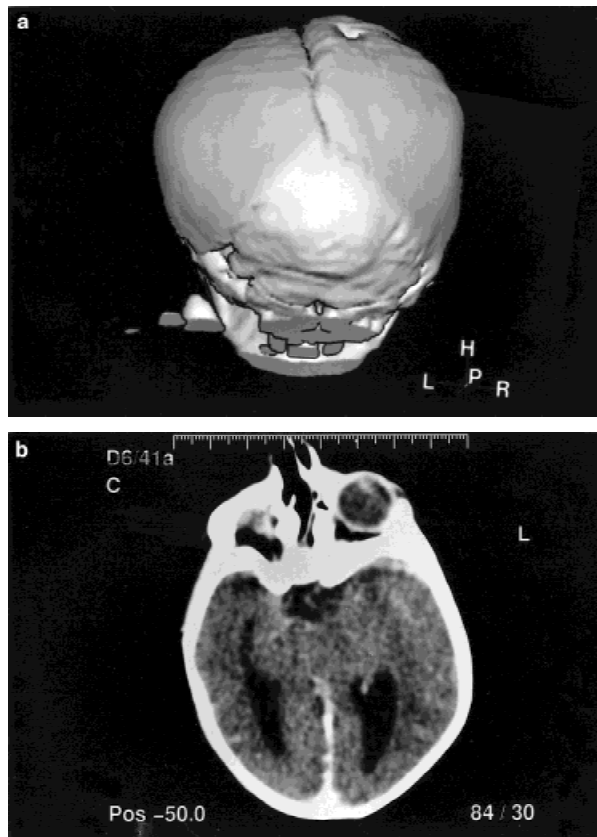


Fig. 5. **a:** A window CT scan of the skull showing small anterior fontanel with lambdoid craniosynostosis. **b:** Brain CT scan showing pachygyria and colpocephalic configuration of the lateral ventricles.

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